RP2

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 12 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: PP#7E3473. Sulfur Dioxide on Grapes.
Amendment of September 13, 1990. **MRID No. 416306-01**
DEB No. 7093. DP Barcode: D156294
HED Project No. 0-1998.

FROM: Martha J. Bradley, Chemist MJ Bradley
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

TO: Walter Francis, PM 32
Disinfectants Branch
Registration Division (H7505C)

and

Toxicology Branch
Health Effects Division (H7509C)

THRU: Robert S. Quick, Section Head RSQ
Tolerance Petition Section I
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

Siemer & Associates Inc. on behalf of Snowden Enterprises Inc. has asked a number of questions related to their SO_2 registration application for the fumigation of grapes in storehouses and trucks. The deficiencies listed in our (E. Haeberer) reviews of February 9, 1989, May 25, 1989 and February 7, 1990 are combined and listed along with the six specific issues addressed in this submission.

A tolerance of 10 ppm has been established for grapes. There is no EPA registration for the use of sulfur dioxide on grapes; however, there is a California state registration for use of sulfur dioxide on grapes. Questions remain to be answered before a US registration is granted.

Deficiencies remaining to be resolved

The nature of the residue in grapes
Secondary residues in meat and milk from irreversibly bound sulfite residues
Enforcement method to determine the total toxic residue
Residues in excess of 10 ppm

Conclusions

1. The nature of the residue in grapes is inadequately defined. Residues on grapes resulting from repeated fumigations with SO_2 gas include free and reversibly bound sulfites, sulfates, and irreversibly bound sulfite residues. The nature of the irreversibly bound sulfite residues is not defined either qualitatively or quantitatively. A radiolabeled metabolism study is needed with repeated, long term exposure of grapes to $^{35}SO_2$.

2. Metabolism and feeding studies indicate that residues of extractable sulfite would be negligible in meat and milk from the proposed use. Evidence indicates that extractable sulfite residues existing in meat and milk to date, are of negligible amount, i.e., <0.005 ppm in milk, and <0.008 ppm in meat. We can draw no conclusions concerning the ingestion of irreversibly bound sulfite residues since neither the nature nor the quantity of the residue is known.

3. An enforcement method cannot be chosen until the nature of the residue on grapes is adequately known. The enforcement method must be able to determine the total toxic residue.

4a. No final conclusions can be drawn concerning the adequacy of the proposed 10 ppm tolerance for the fumigation uses requested in this petition. Some tentative conclusions can be made based on the assumption that the head space - GC method will be validated and that any additional data submitted will not alter the residue picture. The residue values are for combined free and reversibly bound sulfite residues (total residues).

4b. Residue Chemistry concurs that the grape industry keeps sufficient records so that different dosing for different varieties is feasible. It is also reassuring that Thompson seedless grapes, which seem to accumulate sulfites at a higher rate than seeded varieties, have a limited storage life.

4c. The data for the proposed high dosage at weekly intervals use in commercial storage houses do not support more than 12 fumigations, with the maximum concentration of gas for the initial fumigation at 0.5% and subsequent maintenance fumigation

concentrations no greater than 0.25%. The residue levels could exceed the proposed 10 ppm tolerance with a higher number of fumigations and/or higher concentrations of sulfur dioxide gas.

98% of the grapes fumigated in storage from 0 to 9 times with a 24 hour post-gassing interval would have residues <10 ppm and 95% of the residues would be <10 ppm at 4 hours after gassing.

4d. The residues from both truck application methods appear to be comparable, however it would seem that the under-the-pallet method would be less likely to spray the gas on the fruit.

From the limited data, we tentatively conclude that residues from the truck fumigation will be <10 ppm in less than 24 hours after gassing.

4e. From this limited study, we tentatively conclude that residues from the low dosage - high frequency application are not likely to leave residues exceeding 10 ppm.

5. The data generated to support the proposed 10 ppm tolerance level for SO_2 do <u>not</u> address the issue of irreversibly bound sulfite residues. These residues, of unknown composition, may be present in varying concentrations, and are not determined by either the Monier - Williams or head space - GC methods. If significant levels of irreversibly bound sulfite residues are present, then total residues of free sulfite, reversibly and irreversibly bound sulfite residues may be higher than the levels reported in the data submitted.

<u>Note to PM:</u> The registrants last question, No. 4. of Letter of September 13, 1990, deals with the storage of the pesticide containers and is not under the purview of Chemistry Branch. The PM should direct this question to the proper reviewer.

Recommendation

Chemistry Branch I recommends that a copy of this review be sent to the registrant.

Detailed Considerations

Deficiency 1a. The nature of the residue in grapes is inadequately defined. Residues on grapes resulting from repeated fumigations with SO_2 gas include free and reversibly bound sulfites, sulfates, and irreversibly bound sulfite residues. The nature of the irreversibly bound sulfite residues is not defined

either qualitatively or quantitatively. A radiolabeled metabolism study is needed with repeated, long term exposure of grapes to $^{35}SO_2$.

Response 1a. This deficiency has not been addressed by the registrant.

Comments/Conclusions 1a. This deficiency has not been resolved.

Deficiency 2b. Metabolism and feeding studies indicate that residues of extractable sulfite would be negligible in meat and milk from the proposed use. Evidence indicates that extractable sulfite residues existing in meat and milk to date, are of negligible amount, i.e., <0.005 ppm in milk, and <0.008 ppm in meat. We can draw no conclusions concerning the ingestion of irreversibly bound sulfite residues since neither the nature nor the quantity of the residue is known.

Response 2b. This deficiency has not been addressed by the registrant.

Comments/Conclusions 2b. This deficiency has not been resolved.

Deficiency 3a. Most of the residue data presently in this submission have been generated using the head space - gas chromatography method. No conclusions can be drawn concerning the adequacy of the head space - gas chromatography method for the analysis of total SO_2 residues until submission of additional method validation data from a second analytical laboratory. This study is currently in progress. It should be noted that, as with the official modified Monier - Williams method, the head space - GC analytical method does <u>not</u> determine irreversibly bound sulfite residues. The head space method determines free and reversibly bound sulfite residues and differentiates between those residues and hydrogen sulfide.

Deficiency 3b. The method presently used for regulatory purposes is the modified Monier - Williams method. The method determines free and reversibly bound sulfite residues and also hydrogen sulfide. Residue levels found by the Monier - Williams method may be higher than that determined by the head space - GC due to inclusion of hydrogen sulfide in the analysis.

Response 3a and 3b. The registrant states that significant comparative data have been submitted for the Monier - Williams (MW) and the head space - GC method in their June 27, 1938 submission assigned MRID number 40758501. The data generally show that MW is incapable of detecting anything below 2.5-3.0 ppm SO_2, while the GC method easily detects 0.5 ppm SO_2 and

differentiates between SO_2 and H_2S, which the MW does not. The registrant specifically asks whether the Agency will accept the GC methodology if it is validated by an independent laboratory as required in PR Notice 88-5.

Comments/Conclusions 3a and 3b. We cannot verify the assertions of the detection levels of the two methods or that the GC method differentiates between SO_2 and H_2S, which the MW does not since the listed MRID number contains only product chemistry data. While it is true that the Monier - Williams method can detect indigenous sulfur compounds, the use of blank analyses should by used to distinguish the difference from untreated grapes and treated grapes. In the submitted data comparing residue levels by both methods, the Monier - Williams method routinely shows 2 to 3 ppm higher levels than the GC method. There is no indication that blank analyses were used to correct for indigenous sulfur compounds. For the time being, the Monier - Williams method is officially recognized by the FDA as the enforcement method for sulfites on grapes, therefore, the acceptance of a method that routinely shows lower residue levels such as the GC method is impractical. (Unless the registrant can prove that the Monier - Williams method gives erroneous results, EPA cannot accept as an enforcement method any other than FDA's official method.) An enforcement method cannot be chosen until the nature of the residue on grapes is adequately known. The enforcement method must be able to determine the total toxic residue.

This deficiency has not been resolved.

Deficiency 4. No final conclusions can be drawn concerning the adequacy of the proposed 10 ppm tolerance for the fumigation uses requested in this petition. Some tentative conclusions can be made based on the assumption that the head space - GC method will be validated and that any additional data submitted will not alter the residue picture. The residue values are for combined free and reversibly bound sulfite residues (total residues).

1. The data for the proposed use in commercial storage houses do not support more than 12 fumigations, with the maximum concentration of gas for the initial fumigation at 0.5% and subsequent maintenance fumigation concentrations no greater than 0.25%. The residue levels could exceed the proposed 10 ppm tolerance with a higher number of fumigations and/or higher concentrations of sulfur dioxide gas. From the data collected during the 1988 certification program where 1-9 fumigations with dosing ranging from 0.15 to 1%, Chemistry Branch concluded that 98% of the grapes fumigated in storage would have <10 ppm residue 24 hours after gassing and that 95% of the residues would be <10 ppm at 4 hours after gassing.

Although it is true that different grape varieties take on and dissipate residues at different rates, it would not be practical to recommend different use patterns for the many varieties of grapes since they are often stored and treated in the same facility. Additional residue data are being generated by the petitioner and may alter our conclusions.

Response 4-1. The registrant's contention is that the grape industry can keep the varieties separate. The industry keeps records for each pallet of grapes for grower accounting, inventory, shipping and other purposes. Careful records of SO_2 applications for each cold storage room and the amount of SO_2 used is reported to the County Agricultural Commissioner on a monthly basis. Letters from four Agricultural Commissioners from the Counties of Fresno, Kern, Madera and Tulare are submitted stating that the grape industry keeps sufficient records to control the number of fumigations each pallet of grapes receives. One of the Commissioners letters also adds that the normal storage duration of Thompson Seedless Grapes is about two months because they being to break down when stored longer. With the normal gassing schedule of once a week, that would mean that Thompson seedless would as a rule not be exposed to more than eight or nine gassings prior to shipment.

Comment/Conclusions 4-1. Residue Chemistry concurs that the grape industry keeps sufficient records so that different dosing for different varieties is feasible. It is also reassuring that Thompson seedless grapes, which seem to accumulate sulfites at a higher rate than seeded varieties, have a limited storage life.

However, we can only repeat the previous conclusions: The data for the proposed use in commercial storage houses do not support more than 12 fumigations, with the maximum concentration of gas for the initial fumigation at 0.5% and subsequent maintenance fumigation concentrations no greater than 0.25%. The residue levels could exceed the proposed 10 ppm tolerance with a higher number of fumigations and/or higher concentrations of sulfur dioxide gas and 98% of the grapes fumigated in storage from 0 to 9 times with a 24 hour post-gassing interval would have residues <10 ppm and 95% of the residues would be <10 ppm at 4 hours after gassing.

Deficiency 4-3. The labeling for the proposed truck fumigation use must provide detailed directions to avoid the direct spraying of sulfur dioxide on the fruit and assure proper circulation of fumigant throughout the truck.

Response 4-3. The registrant states that it is impractical to impose a 24 hour holding time between truck gassing and shipping.

They further state that the industry certification data showed that the exception of higher than 10 ppm SO_2 residue results were only associated with liquid SO_2 being sprayed directly onto fruit, in which case very high residues resulted. However, the high SO_2 residues found at the point of origin did not result in any crop reaching market with residues above 10 ppm as reanalysis at the destination showed. The registrant adds that during the 1988 certification program, FDA and EPA did not require the testing of grapes that had been fumigated once by truck or 1-3 times in cold storage. This action was supported by 100 samples collected from each treatment regimen. This action is what led to the proposed wording on the label that grapes gassed less than four times would not be subject to a 24 hour holding period.

The registrant proposes the gassing of trucks by placing the gas induction tube under one of the rear most pallets and fastening it with a staple to the pallet. The gas would be introduced under the packed fruit instead of the usual administration of the gas vertically up the back of the load, between the closed door and the loaded fruit. The registrant requests that a study, Assessment of SO_2 Residue Accumulation in Grapes Fumigated in Truck Trailers Vol. 1 & 2 (Lab I.D. 40049-10-87) MRID 40758501 be considered for the truck gassing use. Data on the use of the tube for gas introduction, collected by the California Table Grape Commission and Snowden is submitted.

Comment/Conclusion 4-3. FDA, (letter of March 10, 1988 from L. Robert Lake, Director, Office of Compliance, Center for Food Safety and Applied Nutrition to the California Table Grape Commission), required spot checking of 100 samples from truck fumigations and 100 samples from warehouse fumigations for grapes fumigated one to three times with other conditions related to the previous year's sampling and the proviso that the grapes contain <10 ppm residue.

The study identified incorrectly by the registrant as MRID 40758501 was reviewed in our (E. Haeberer) memo of February 9, 1989. The study was conducted on Flame seedless grapes by administering the gas vertically up the back of the load and provided comparative data for the Monier - Williams and GC methods. The samples were taken 1 hour after treatment of 0.75 or 1% gassing. Residues ranged from 0.8 to 4.9 ppm by the Monier - Williams method.

The new study, Sulfur Dioxide Residues In Perlette Table Grapes Fumigated With Sulfur Dioxide in Refrigerated Truck Trailers - A Test Of Different Methods For Release Of The Fumigant dated May 21, 1988, consists of eight trailers loaded with Perlette table grapes fumigated with a standard truck shot of 3.5 pounds of sulfur dioxide. Three trucks were fumigated using the hollow wand and directing the gas above and between

pallets. Five trucks were fumigated using a tube to direct the gas under the pallets. Samples were taken one hour after the fumigation from sampling boxes (unpalletized) from the trucks. The Monier - Williams method was used for the analyses. Residues from the samples treated by the over-the-pallet method ranged from 2.1 to 5.9 ppm while residues from under-the-pallet method ranged from 1.2 to 6.5 ppm. The residues from both truck application methods appear to be comparable, however it would seem that the under-the-pallet method would be less likely to spray the gas on the fruit.

From the limited data, we tentatively conclude that residues from the truck fumigation will be <10 ppm in less than 24 hours after gassing.

Deficiency 4-4. The data generated to support the proposed 10 ppm tolerance level for SO_2 do not address the issue of irreversibly bound sulfite residues. These residues, of unknown composition, may be present in varying concentrations, and are not determined by either the Monier - Williams or head space - GC methods. If significant levels of irreversibly bound sulfite residues are present, then total residues of free sulfite, reversibly and irreversibly bound sulfite residues may be higher than the levels reported in the data submitted.

Response 4-4. The registrant has not responded to this deficiency.

Comment/Conclusion 4-4. The deficiency has not been resolved.

Low Dosage - High Frequency Application

The registrant has proposed an additional treatment regimen for storehouse; use of low dosage - high frequency application. The studies were previously submitted commingled with high dosage applications. The results from the low dosage - high frequency application have been isolated and resubmitted. Thompson Seedless, Flame Seedless, Christmas Rose and Emperor grapes were tested and analyses were conducted using the GC method. The grapes, some initially treated at 8000 to 10,000 ppm were stored in three facilities for up to 16 weeks with a maximum of 47 applications of 200 to 400 ppm sulfur dioxide three times a week. The grapes were sampled at 2 week intervals. Residues from 124 analyses ranged from <0.5 ppm to 6.5 ppm. The highest residue resulted from a seedless variety after 14 weeks of treatment and the grapes had started to deteriorate. The statement is made that the quality of seedless varieties tended to deteriorate after 10 to 12 weeks in storage.

From this limited study, we tentatively conclude that residues from the low dosage - high frequency application are not likely to leave residues exceeding 10 ppm.

Note to PM: The registrants last question deals with the storage of the pesticide containers and is not under the purview of Chemistry Branch. The PM should direct this question to the proper reviewer.

cc: M Bradley, RF, Circu, PP#7E3473, PIB/FOD(Furlow), R Schmitt
H7509C:CBTS:M Bradley:CM#2:Rm810:557-7324:06/24/91
RDI:RSQuick:08/07/91:RALoranger:08/08/91